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Integration of filgrastim into chemoradiation for limited small c lung cancer: a Phase I study.

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PURPOSE: Recent studies document the value of early combined modality t of small cell lung cancer, but also indicate that early thoracic radiation adds t myelosuppression and can complicate further chemotherapy. Other studies ir that simultaneous use of growth factors with thoracic radiation may be delete However, temporal separation of growth factor use from cytotoxic therapy m allow dose intensity to be maintained/enhanced during combined modality treatment. We sought to integrate filgrastim into a novel chemoradiation regi for patients with limited small cell lung cancer using an approach that separa growth factor administration from both chemotherapy and thoracic radiation. METHODS AND MATERIALS: Twenty-seven patients with limited disease small cell lung cancer were enrolled in a Phase I trial of cisplatin, ifosfamide/mesna, oral etoposide, and thoracic radiation (1.5 Gy b.i.d. x 30 fractions days 1-19 cycle 1) +/- filgrastim (5 microg/kg/day). Filgrastim was on days 20-25 of cycle 1 after completion of radiation and following complet oral etoposide in subsequent cycles. The primary end point was determinatio maximum tolerated dose (MTD) of chemotherapy. Serial cohorts were treate and without filgrastim. RESULTS: Because of dose-limiting thrombocytope primarily, and nonhematologic toxicity, the MTDs with and without filgrasti were identical (cisplatin 20 mg/m2 i.v. and ifosfamide 1200 mg/m2 i.v., both days 1-3, and etoposide 40 mg/m2 p.o. days 1-14). Filgrastim use shortened duration of neutropenia at the MTD (median 4 vs. 7 days), but was not assoc with a reduction in febrile neutropenia. Although growth factor administratio not allow dose escalation of this regimen, it did allow chemotherapy doses to maintained at the MTD more frequently through four cycles of therapy. In th evaluable patients, the overall response rate was 100% (71% partial and 29% complete). CONCLUSIONS: Despite careful attention to the timing of growt factor with chemoradiation, the administration of filgrastim with this regimen not allow dose escalation. As in many other recent studies of hematopoietic g

factors given prophylactically with chemotherapy, the duration of neutropeni the MTD was shortened and the need for dose reduction throughout treatmen reduced in patients receiving filgrastim at the MTD.

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